Serial No. 09/496,44
Group Art Unit: 1638

REMARKS/ARGUMENTS

The Examiner rejects claims 2-18, 23-25, 27-53, 64, 66-69 and 71-74 under 35 U.S.C. 112, first paragraph, for written description.

The Examiner maintains that reciting the polynucleotides have at least 80% identity to SEQ ID NO: 1 does not describe the structural features common to polynucleotides having at least 80% identity to SEQ ID NO:1 that are capable of modulating the level of cyclin E protein in a cell.

Applicant respectfully submits that amended Claim 64 requires the combination of function and structure which are sufficient to meet the written description requirement. The claims have been amended to recite "An isolated nucleic acid that modulates the level of cyclin E". As discussed in previous responses, the % homology and the activity of the isolated nucleic acid can be readily determined.

When determining the quantity of experimentation necessary, the focus is not on the amount of experimentation necessary to practice the entire genus, but the amount of experimentation required to practice any particular member. This concept is the central holding of In re Wands, 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988), where the claims read on the use of any IgM antibody that possessed a particular binding affinity.

The Examiner states that Example 9 of the USPTO Written Description Guidelines describes hybridizing nucleic acids that were not sequenced but "several were shown to encode proteins that bind to dopamine receptor and stimulate adenylate cyclase activity." The Examiner states that the Applicants have not disclosed a sequence with at least 80% identity to SEQ ID NO: 1 that is capable of modulating the level of cyclin E protein in a cell.

The Applicant submits that one of ordinary skill in the art would be able to change the identity of SEQ ID NO: 1 by up to 20% and then screen the changed sequences to obtain isolated nucleic acids that "modulate the level of Cyclin E

protein in a cell. The fact that the sequences have not been created does not prevent them from being protected in this manner. As stated in MPEP 2163 (3) (a), "An invention may be complete and ready for patenting before it has actually been reduced to practice."

The Examiner argues that, "Since a change in even a single nucleotide has the potential to alter the amino acid sequence of a polypeptide encoded by a polynucleotide, the Examiner maintains that polynucleotides requiring 80% identity to SEQ ID NO: 1 do read on widely variant species.

Applicants respectfully disagree. The claims require that the isolated nucleic acid modulate the level of cyclin E and have at least 80% identity to the entire coding region. If a nucleic acid does not, then the nucleotide does not fall within the scope of the claims. Based on the disclosed sequence, one of skill in the art can easily make nucleotide changes that maintain the function of cyclin E. Silent and conservative variants can readily be determined by one of skill in the art. Functional sequences can be obtained by using primers based on the present claimed sequence. Applicants believe the inventors deserve to protect their invention and that one of ordinary skill in the art would be able to make and use the invention as claimed given the written description of this application.

The Examiner rejects claims 2-18, 23-25, 27-53, 64, 66-69 and 71-74 under 35 U.S.C. 112, first paragraph, for enablement.

The Examiner states that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims. The Examiner maintains that the disclosure of methods to identify compositions and assays to determine their functionality does not provide sufficient guidance for one skilled in the art to determine, without undue experimentation, which isolated nucleic acids encode a protein that could be used to practice the claimed invention.

The USPTO carries the initial burden to establish a reasonable basis for questioning the enablement provided for the claimed invention. As stated in In re Wright, 99, F.2d 1557, 27 USPQ2d 1510 (Fed. Cir. 1993); MPEP § 2164.04, the enablement requirement is satisfied if the specification describes any method for making and using the claimed invention that bears a "reasonable correlation" to the entire scope of the claims. Applicants submit that this has been accomplished in the present application.

Sequences obtained with less than 100% identity could easily be tested for activity using the methods outlined in the present application. "That one skilled in the art must perform some preliminary tests or experiments before he can make or use the invention does not invalidate the patent" on the basis of section 112. Atlas Powder Co. v. E. I. Du Pont De Nemours & Co., 750 F.2d 1569, 1576 (Fed. Cir. 1984). Thus, polynucleotides having less than 100% identity, which also encode for functional CycE polypeptides, can easily be found without undue experimentation.

In *Amgen v. Chugai* the Federal Circuit held that "Conception does not occur unless **one has a mental picture of the structure of the chemical, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it**" *Amgen v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ1016, 1021 (Fed. Cir. 1991). See also *Ex parte Maizel*, 27 USPQ2d 1662, 1669 (B.P.A.I. 1992), citing Amgen v. Chugai, 927 F.2d 1200, 1206 (Fed. Cir. 1991).

Claims 64, 66 and 71 require an isolated nucleic acid comprising a polynucleotide having at least 80 % identity to SEQ ID NO: 1. The claims also require that the isolated nucleic acid modulates the level of Cyclin E protein. Conserved regions required for Cyclin E protein activity are defined in the present specification. The method of preparation of the claimed nucleic acids and their physical or chemical properties are disclosed in the present application.

In *University of California v. Eli Lilly and Co.* the Federal Circuit held that "description of a genus of cDNAs may be achieved by means of a recitation of a

representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus **or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus"**, *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

The limitations of present claims focus on structural features such as percent identity with the added requirement of the function of modulating the level Cyclin E protein. These structural features are readily understood by those skilled in the art and are fully supported by the specification as noted in the Appeal Brief dated March 18, 2003, pages 11-15.

The Examiner goes on to state that, "the disclosure of a single functional polypeptide sequence of SEQ ID NO: 1 does not support the enablement of sequences having at least 80% identity to SEQ ID NO: 1 because the specification does not provide sufficient guidance for discriminating between operative and inoperative embodiments that fall within the scope of the invention."

The Applicants point out that in Example 9 of the USPTO Written Description Guidelines it states that "several" hybridizing nucleic acids were shown to have activity. Though not explicitly mentioned in the example, one of ordinary skill in the biological sciences would know that a number of hybridizing nucleic acids would not have activity. Thus screening for activity among the hybridizing nucleic acids is necessary to obtain "several" functional nucleic acids. Example 9 clearly requires a screening process, which discriminates between the operative and inoperative embodiments.

This is the circumstance with the present invention. The specification clearly states how one can change SEQ ID NO: 1 to achieve nucleic acids having at least 80% identity and the specification clearly states how to screen those nucleic acids to obtain a functioning cyclin E. See the bottom half of page 7 and the top half of page 8 of the response filed March 18, 2003 for examples in the specification on how to make variants of the sequence. The screening for a cyclin E that binds to Cdk2 and

Rb proteins can be done through protein binding experiments known to one of ordinary skill in the art (see the specification, top of page 33).

The Examiner goes on to state that, "Guidance for making and using the claimed invention is also necessary for enablement because it is unpredictable whether expression of the claimed polynucleotides in plant cells or plants would result in any of the claimed effects of cell divisions, cell growth, crop yield, organ growth, etc. The claimed effects are unpredictable because the prior art teaches that progression through the cell cycle, including the G1 to S transition, is affected by the activity of numerous proteins in addition to cyclin E. Furthermore, cyclin E itself does not act independently. ...It is unpredictable whether the various proteins that positively and negatively influence cyclin E function would be present in plant cells at the appropriate time, in the appropriate place, and in the appropriate quantity such that expressing the claimed polynucleotides would result in the desired phenotypic effects."

While it is true Cyclin E does not act independently, this is true of most proteins in biological systems. The lack of independence in itself does not make the effects any more or less unpredictable. When a functional isolated nucleic acid of claims 64, 66 and 71 is introduced into a typical plant cell, the regenerated plant will provide the machinery necessary for the isolated nucleic acid to function as predicted. The Examiner has provided no evidence to the contrary.

The Examiner goes on to state that, "The claimed effects are also unpredictable because the prior art teaches that the effect of overexpressing cyclin E is unpredictable. For example, Sgambato et al. teach that over expression of the same cyclin E cDNA in different cell types produces different biological effects."

The Applicants point out that in the same article on page 1397, second full paragraph, it states that, "The divergent effects of this cyclin E cDNA in different cell types are not surprising since there are several other examples in which cell context influences the action of other gene involved in growth control." Once again the specification, on pages 9-12 and 30, discloses that different desired effects require

different tissues and promoters in order to obtain the desired effects of modulating cyclin E protein.

The Examiner rejects claims 23-25, 27-33, 35-37, 39-64, and 71 and the claims dependent thereon under 35 U.S.C. 112, second paragraph, for being indefinite.

The Examiner rejects claims 23, 39-41, 44-64 and 71 for the use of the term "modulating." The Examiner states that the term is relative and there is no comparative basis.

Applicants have amended the claims. The Claims now recite a comparative basis.

The Examiner rejects claim 23 for the recitation of "time sufficient to induce expression of the polynucleotide sufficient to modulate CycE protein in the cell."

Applicants have amended the claim. It now is in form for allowance.

The Examiner rejects claims 27, 30, 36, 46, 47, and 51 for the use of the term "alter" because it is a relative term that lacks comparative basis.

Applicants have amended the claims. The Claims now recite a comparative basis.

The Examiner rejects claim 27 for the recitation of "an amount of time sufficient to alter cell division" because the metes and bounds of the phrase are unclear.

Applicants have amended the claim. It now is in form for allowance.

The Examiner rejects claims 28, 32, 35, 43, 45 49, 50, and 53 for the use of the term "increase" because the term is relative and lacks comparative basis.

Applicants have amended the claims. The Claims now recite a comparative basis.

The Examiner rejects claim 28 for the recitation of "an amount of time sufficient to alter cell division" because the metes and bounds of the phrase are unclear.

Applicants have amended the claim. It now is in form for allowance.

The Examiner rejects claim 28 because there is not proper antecedent basis for "cells" in claim 23 from which it depends.

Applicants have amended the claim. The claim now has proper antecedent basis.

The Examiner rejects claims 29 and 48 because the term "improve" is a relative term that lacks comparative basis.

Applicants have amended the claims. They are now in form for allowance.

The Examiner rejects claim 29 because of the recitation of "an amount sufficient to improve transformation frequencies."

Applicants have amended the claim. It now is in form for allowance.

The Examiner rejects claim 30 because of the recitation of "an amount sufficient to alter cell growth."

Applicants have amended the claim. It now is in form for allowance.

The Examiner rejects claim 31 because of the recitation of "positive growth advantage."

Applicants have amended the claim. It now is in form for allowance.

The Examiner rejects claim 32 because of the recitation of "an amount sufficient to increase growth rate."

Applicants have amended the claim. It now is in form for allowance.

The Examiner rejects claim 33 because of the recitation of "wherein the cell is a plant cell" and the claim from which it depends already requires the transforming of a plant cell.

Applicants have amended the claim. It is now in proper form for allowance.

The Examiner rejects claim 33 because of the recitation of "capable of expressing CycE protein". The Examiner states that the claim is unclear because any regenerated plant would inherently possess the capability of expressing a CycE protein.

Applicants have am nded the claim. It is now in proper form for allowance.

The Examiner rejects claim 35 because of the recitation of "an amount sufficient to increase crop yield."

Applicants have amended the claim. It is now in proper form for allowance.

The Examiner rejects claim 35 because of the recitation of "an amount sufficient to alter plant height or size."

Applicants have amended the claim. It is now in proper form for allowance.

The Examiner rejects claims 37 and 42 because of the recitation of "enhance." The Examiner states that the term lacks comparative basis and it is unclear what type of enhancement is intended.

Applicants have amended the claims. They are now in proper form for allowance.

The Examiner rejects claim 37 because of the recitation of "inhibit."

Applicants have amended the claim. It is now in proper form for allowance.

The Examiner rejects claim 42 because of the recitation of "embryogenic response." The Examiner states that it is unclear what type of embryogenic response the claim encompasses.

The Applicants have amended the claim to recite "embryos from the transformed plant have an increase in embryogenic response when compared to embryos from a control plant that are cultured under the same conditions."

The Examiner rejects claim 42 because of the recitation of "an amount sufficient to enhance embryogenic response".

Applicants have amended the claim. It is now in proper form for allowance.

The Examiner rejects claim 43 because of the recitation of "an amount sufficient to increase callus induction".

Applicants have amended the claim. It is now in proper form for allowance.

The Examiner rejects claim 48 because of the recitation of "the response of cells to environmental stress". The Examiner states that it is unclear what type of environmental stress response the claim encompasses, as cells may respond differently to a variety of stresses.

Applicants have amended the claim. The claim now states, "wherein the level of CycE protein is modulated to increase the viability of the cell when placed under environmental stress including dehydration, heat, or cold when compared to a corresponding non-transformed plant cell placed under the same stress."

The Examiner rejects claims 16-18 under 35 U.S.C. 101 and 35 U.S.C. 112.

The Examiner maintains the rejection of claims 16-18 under 35 U.S.C. 101 as not being supported by a specific and substantial utility, for reasons of record set forth in the office action mailed September 20, 2002. The Examiner states that Applicants have not demonstrated, and the prior art does not teach, a specific and substantial utility for plants or plant cells that express a polynucleotide of SEQ ID NP:1, or for plants or plant cells that express a polynucleotide encoding an E-type cycling

Claims 23-53 present specific and substantial utilities for CycE nucleic acids. The 1.132 Declaration filed June 28, 2001 provides evidence that the claimed sequence is a CycE nucleic acid. The Examiner has not provided any evidence that the claimed nucleic acids will not function as predicted.

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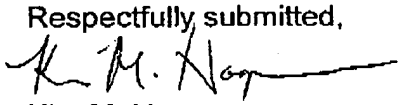
CONCLUSION

Applicant submits that in light of the foregoing amendments and the remarks, claims 2-18, 22-53, and 64-75 are in condition for allowance. Reconsideration is respectfully requested. If it is felt that it would aid in prosecution, the Examiner is invited to contact the undersigned at the number indicated to discuss any outstanding issues.

Respectfully submitted,



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